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14. ABSTRACT Six academically qualified students, 3 each from Delaware St. University (DSU) and Lincoln University, were offered slots in the PCR program. Five accepted: 3 from Lincoln and 2 from DSU. Students did 10-week research rotations in addition to attending research seminars and roundtable discussions on the basis of health disparities. This latter topic was not in the initial grant but was received favorably. Students presented research posters in a joint undergraduate research symposium at the end of the summer with almost 200 other students from several summer student research programs. In a poster session at Lincoln University, our DoD students swept the prizes for biology I group competition. Students also took their posters to other national meetings. Graduating students from Lincoln University and Del. St. University are applying to Graduate Schools for post-baccalaureate education. One still intends to apply to Medical School. The PI, Co-PI and a mentor (Cooper) gave prostate and health disparity lectures at Lincoln University and Delaware State University in 2006. This will continue in 2007. In addition, outside speakers of prominence are being recruited to speak in the program.					
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Introduction:

Due to the extremely low levels of minority faculty and graduate students in the sciences, the DoD Majority Institution (MI) /Historically Black College and University (HBCU) program was intended to foster and promote the interest of minority students in basic science and research by coupling a one or more HBCU with a sponsoring MI. In Delaware, this has been accomplished by coordinating student recruitment, for stipended summer research, from Delaware State University and Lincoln University to perform research in prostate cancer laboratories at the University of Delaware. Our Aims were to 1) offer a 10-week summer research program to 5 qualified minority students, 2) Offer a summer enrichment program to these students and 3) offer activities and extended research at the participating HBCUs during the following academic year.

Body:

In compliance with Aim 1, and upon the recommendation of the faculty campus coordinators at Delaware State and Lincoln Universities, three students from Lincoln and three students from Delaware State University were chosen for admission into the University of Delaware's training program in Prostate Cancer. One student from Delaware State University, Feh Fombi, subsequently accepted a summer position at Ohio State. Each student was recognized by the campus coordinator as being academically excellent (3.0 grade point average or above) and motivated to do research. Students in the program participated in research for 10 weeks during the summer and attended weekly seminars related to research

<http://www.udel.edu/chem/white/HHMI2/S06/S06enrichment.html>.

In compliance with Aim 2, in addition to doing bench research, students attended additional discussion sessions on the topic of *Healthcare Disparities*. These discussion sessions were not proposed in the grant but were quite successful as judged by a survey that students were required to fill out. Prior to each session students were assigned to read both popular and scientific literature regarding the socio-economic or medical causes of healthcare bias. UD faculty from the Departments of Biological Sciences, Chemistry and Biochemistry and Philosophy led the discussions.

At the end of the summer program, each student presented the results of their research at the University's undergraduate research symposium. The symposium was modeled after the Experimental Biology meeting, where posters and talks occurred simultaneously and where there was a plenary lecture by a Howard Hughes Medical Institute investigator

<http://www.udel.edu/chem/white/HHMI2/Symp06/S06symposium.html>. The titles of the presentations for students in our program were as follows:

Renee Dixon (Lincoln University); *The Development of an Animal Model for the Analysis of Novel Therapeutic Anti-Metastatic Agents*. (Mentor: Dr. Robert Sikes)

Candice Johnson (Lincoln University); *The Effects of Voltage Sensitive Calcium Channels on Proliferation of Prostate Cancer Cells*. (Mentor: Dr. Randall Duncan)

Lauretta Ovadge (Lincoln University); *The Search for Genes in Prostate Morphogenesis*. (Mentor: Dr. Robert Sikes)

Erin Stallings (Delaware State University); *SPAM-1 Expression in Prostate Cancer Cell: A Possible Adhesion Marker for Metastatic Tumors*. (Mentor: Dr. Patricia DeLeon)

Noella Zony (Delaware State University); *IGF-1 Influences CD44 Expression in Human Prostate Cancer*. (Mentor: Dr. Carlton Cooper).

*See Appendix for Abstracts.

In compliance with Aim 3, following the summer experience, activities returned to the HBCU campuses. Several of the students made significant progress with their research during the fall semester. Renee Dixon, Candice Johnson, and Laurette Ovadje, were able to commute to the University to do their research. In addition, Lincoln University students participated in a poster competition held for all students in the sciences, about 20, who participated in research over the summer. In the Biology I group first, second and third prizes went to Candice Johnson, Renee Dixon and Lauretta Ovadje respectively from 7 students. Lauretta Ovadje also presented a revised poster of the same title to 2006 Annual Biomedical Research Conference for Minority Students (ABRCMS) in Los Angeles and Renee Dixon presented a revised version of her poster with the same title to a minority student symposium in Florida. Erin Stallings also participated in the 2006 ABRCMS meeting and presented her poster on SPAM-1. Also, during the fall semester, Drs. Robert Sikes, Carlton Cooper and David Usher gave talks at each University, once in September, October, and November or December. The titles of the lectures were, *The Terminal Stages of Obesity* (Usher), *The Prostate Cancer Primer* or *Everything you wanted to know about prostate cancer but were afraid to ask*. (Sikes), *Health Disparities of Prostate Cancer* (Cooper).

Reportable Outcomes:

In addition to the aforementioned posters, poster session attendance, and poster presentations at national meetings, each student was recently asked about their plans for coming year since the programs' research experience is meant to foster an interest in research. Candice and Lauretta will be graduating from Lincoln University in May. Candice has applied to graduate school and Lauretta has applied to graduate school for public health and epidemiology. Renee plans on applying to medical school. At DSU both Erin and Noella have applied to graduate schools for biomedical research and Chemistry or Pharmacology respectively.

We are currently in the recruiting stage for the upcoming summer program. We have identified the following laboratories as possible placements at the University of Delaware: Dr. Sikes, Dr. Cooper, Dr. Koh, Dr. DeLeon, Dr. van Golen (new), and Dr. Duncan. This year students have an expanded choice of projects and destination laboratories. To this end we have had student faculty recruiting meetings at Lincoln University with a scheduled meeting at DSU later this month.

Conclusions:

The program seems to be off to an admirable start. Apparently, we have some changes required to increase communication between faculty involved in research at the MI and the NBCU during the academic year. Coordination of research projects consistent with the capabilities of the HBCU is definitely required to minimize student commuting during the academic year and maximize research productivity at the HBCUs.

Overall, we have altered the number of minority students applying to graduate schools instead of medical schools as indicated by their initial interests coming into the program. Whether the research year has changed their mind in this regard will have to be determined but was not part of the original aims of the program.

References:

Not Applicable to date.

Appendices: Student Abstracts

The Development of an Animal Model for the Analysis of Novel Therapeutic Anti-Metastatic Agents

Renee Dixon, 1 Jamie Fiske, 2 Samantha Allen, 2 David J. DeGraff, 2 and

<<http://www.udel.edu/bio/people/faculty/rsikes.html>>Robert A. Sikes 2

1 Department of Biological Science, Lincoln University, Lincoln, PA

2 Cancer Ontogeny and Therapeutics Laboratory in the Department of Biological Sciences, University of Delaware, Newark, DE

There are limited models to study the spontaneous metastasis and bone colonization of prostate cancer (PCa). Current mouse models require orthotopic injection and more than six months to form metastasis in bone, with successful lesion formation only 15%-20% of the time. Similarly, intracardiac injection results in variable bone metastases. We hypothesized that under normal gravitational load, the human skeleton has a higher rate of bone turnover than rodents, thus releasing a greater magnitude of bone-derived growth factors necessary for the successful formation of metastatic lesions. Therefore, by using hindlimb suspension to increase bone turnover in mice, this period of high resorptive bone activity will enhance the ability of circulating PCa cells to colonize bone. If successful, this model will allow for the direct analysis of therapeutic agents, such as sodium channel modulating agents or bisphosphonates on cancer metastasis. SCID/bg mice were subjected to three weeks of tail suspension, followed by intracardiac injection of C4-2 PCa cells and a return to normal weight bearing activity. Nine weeks post injection, 100% (8/8) of the mice demonstrated detectable serum PSA levels. These findings suggest that unloaded SCID/beige mice undergo bone remodeling thus enhancing the ability of PCa cells to colonize the bone. Funding by the Department of Defense HBCU/MI Undergraduate Research Training Grant, PC05136.

The Effects of Voltage Sensitive Calcium Channels on Proliferation of Prostate Cancer Cells.

<<http://www.udel.edu/chem/white/HHMI2/S05/HHMIS05.html#Johnson>>Candice M. Johnson1, and <<http://www.udel.edu/bio/people/faculty/rduncan.html>>Randall L. Duncan2

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Intracellular calcium signaling plays a major role in the mitotic cell cycle, thereby influencing cell proliferation. Many types of cancers, including prostate cancer, have been characterized by aberrant calcium signaling occurring in environments which are calcium rich. In this study, we

postulated that increased expression of voltage sensitive calcium channels (VSCC) would result in increased proliferation of prostate cancer cells in the LNCaP progression model and that inhibition of these channels would attenuate proliferation of these cells. LNCaP and C42-B4 cells were seeded in 6 well plates (100,000 cells/well). Using the L-type Voltage Sensitive Calcium Channel (L-VSCC) inhibitor nifedipine, and the T-type Voltage Sensitive Calcium Channel inhibitor sTFX (sitafoxacin), the effects of channel inhibition on proliferating cells were observed. Inhibitors were added after 12 hours. No inhibitor was added to control wells. After each 24 hour period, cells were counted using a hemacytometer and the results graphed. The total duration of the study was 96 hours. Preliminary results suggest that both Nifedipine and sTFX effectively decrease proliferation rates in LNCaPs and C42-B4s. However, the effects are temporal and cell specific along the progression model. sTFX has a more rapid effect than nifedipine on LNCaPs; however, nifedipine becomes more effective after 48 hours. In C42-B4 cells however, nifedipine varies in its effect whilst sTFX steadily attenuates growth. This indicates a change in the expression of the $\alpha 1$ subunit of the calcium ion channels and a modification in the expression of L-type and T-type currents along the LNCaP progression model. RT-PCR and Western Analysis will be carried out in order determine the degree of expression and production of the $\alpha 1$ subunit of the calcium ion channels in LNCaP and C42-B4 cells. This project was funded by the Department of Defense.

The Search for Genes in Prostate Morphogenesis

Lauretta Ovadje¹, <<http://myprofile.cos.com/nelsonab14>>Peter S. Nelson², Cynthia Qian³, <<http://www.udel.edu/bio/people/faculty/rsikes.html>>Robert Sikes³

¹Department of Biology, Lincoln University, PA,

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The Urogenital Sinus (UGS) is predetermined to make the prostate gland at embryonic day 15 (E15). The resulting glandular morphogenesis occurs via epithelial budding from both the ventral and dorsal portions of the UGS to give rise to ventral and dorsolateral lobes of the prostate, respectively. The anterior lobe epithelium buds through Wölffian duct mesenchyme. These differences result in different branching patterns and protein expression profiles in the adult tissue of each prostate lobe. We have undertaken a study to determine the regional differences in gene expression of the UGS in order to assemble a Venn diagram of gene expression. Over 8500 UGS genes and 776 prostate genes were assembled into a cDNA microarray. RNA expression profiling was done on microdissected UGS tissue to yield microarray data from UGS mesenchyme (UGM), UGS epithelium (UGE), dorsal half of UGS (dugs) and the ventral half of the UGS (vUGS). Bioinformatics was then utilized to determine which genes are specifically localized to each compartment. Supported by DoD.

SPAM1 Expression in Prostate Cancer-a Possible Adhesion Marker for Metastatic Tumor

Erin Stallings, <<http://www.udel.edu/chem/white/HHMI2/S06/HHMIS06.html#Stokes>>Brittany Stokes, Mehrnoosh Soori, Minghai Shao,

<<http://www.udel.edu/bio/people/faculty/dgalileo.html>>Deni Galileo,

<<http://www.udel.edu/bio/people/faculty/pdeleon.html>>Patricia A. Martin-Deleon

Department of Biological Sciences

Sperm adhesion molecule 1 (SPAM 1 or PH-20) is encoded by the SPAM 1 gene and is a widely conserved mammalian sperm membrane protein with multifunctional roles in fertilization, and it is best known for its neutral hyaluronidase activity. The human SPAM 1 gene, which is located on chromosome 7q31, is expressed in a variety of cancers in both reproductive and non-reproductive organs where it is up-regulated with abundant transcript levels. However, its protein has never been studied in any malignant cells. The objectives of this study are to (1) document the presence of SPAM 1 protein in prostate cancer lines A and C, previously proven to contain SPAM 1 mRNA by RT-PCR; (2) sub-localize the protein in the cells; and (3) verify its expected hyaluronidase activity. A 64 kDa SPAM 1 protein was detected by Western analysis and confirmed by immunocytochemistry (ICC), which revealed the localization of the protein in the cytoplasm, but not on the plasma membrane. Absence of the protein on the plasma membrane was confirmed by Fluorescence Activated Cell Sorting (FACS), which showed no increase in fluorescence in samples treated with SPAM1 antibody compared to pre-immune serum. Lastly, Hyaluronic Acid Substrate Gel Electrophoresis (HASGE), used to detect hyaluronidase activity of the SPAM 1 protein, revealed the absence of hyaluronidase activity at neutral pH.

Preliminary data suggest that SPAM1 may exert its effect in prostate cancer metastasis via its adhesion properties rather than its enzymatic function, as previously reported. Funded in part by the Department of Defense Grant (DOD)

IGF-1 Influences CD44 Expression in Human Prostate Cancer Cells

Noella M Zony¹ and Lynelle Thorpe²

¹ Biological Sciences, Delaware State University,

² Cancer Biology Laboratory, University of Delaware, Biological Sciences.

CD44 is a multifunctional cell surface adhesion molecule that has been implicated in tumor cell invasion and metastasis. Many cancer cell types, including prostate cancer cells, express high levels of CD44. IGF-1 (Insulin-like growth factor 1) is a polypeptide involved in epithelial cell proliferation and survival that has been shown to play a role in prostate cancer progression. However, the effect of IGF-1 on CD44 expression has not been examined previously in lineage related cell lines of increasing metastatic potential. Therefore we examined the relative expression levels of CD44 in the LNCaP human PCa progression model using Western Blot analysis in order to determine if IGF-1 stimulation affects CD44 expression. Analysis of CD44 protein levels indicated similar levels of CD44 in all cell lines of the LNCaP progression model with higher levels observed in the unrelated PC-3 cell line. Treatment of LNCaP, C4-2, C4-2B4 and PC-3 cell lines with IGF-1, 2ng/ml for 24hours, was done and Western Blot analysis performed to examine CD44 levels. The results indicated a downregulation of CD44 in metastatic C4-2 cells when treated with IGF-1 and an upregulation of CD44 in LNCaP cell lines after treatment with IGF-1. CD44 expression in PC-3 cells was not affected by IGF-1 treatment. These data support previous results that indicate altered regulation of IGF-1 and androgen signaling in the LNCaP progression model and a correlation of high CD44 expression in metastatic prostate cancer.